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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,816	08/20/2003	Charles R. Cantor	25491-2408B	7901

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EXAMINER	
WONG, JENNIFER SHIN SHIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 04/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,816	CANTOR ET AL.	
	Examiner	Art Unit	
	Jennifer Wong	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *March 6, 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *May 13, 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-3, 12-14, in the reply filed on March 6, 2006 is acknowledged.

Information Disclosure Statement

2. The information disclosure statement filed December 24, 2003 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it does not provide an English translation of Japanese Patent No. 635030 (reference Q). It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

3. The information disclosure statement filed May 20, 2003 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it does not provide an English translation of foreign patents DE196180 , DE197314, DE4431174, and

DE4438630 (references HN,HO, IA, IB respectively). Other foreign patents have been such as those listed have been considered to the extend of the English abstract or equivalent has been provided (References HL-HM, HP, HY, HZ, IC, IW). It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because do not recite a clear nexus between the preamble of the claims and the process of the claims. The claims are drawn to "a plurality of target nucleic acid molecules." However, method step a is drawn to "the target nucleic acid," and method step c is drawn to "target nucleic acid molecules." The claims do not clearly set forth the relationship between a plurality of target nucleic acid molecules and

a target nucleic acid. Thereby, it is unclear as to whether the claims are intended to be limited to methods identifying a plurality of target nucleic acid molecules or a target nucleic acid.

Claim 1 broadly recites mass matched nucleotides. However, claims 3 and 14 which are dependant on claim 1 recite "mass matched nucleotide." Accordingly, it is not clear as to whether the claims are intended to be limited to mass matched nucleotides or a mass matched nucleotide.

Accordingly, one skilled in the art cannot determine the meets and bounds of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-3, 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Koster (U.S. Patent No. 5,547,835, published August 20, 1996).

With respect to claim 1, Koster teaches methods for identifying nucleotides at one or more base positions in a plurality of target nucleic acid molecules. By determining the mass difference of each nucleotide, a sequence of a target nucleic acid can be determined by the identity of each nucleotide base. Koster teaches each of the

four different nucleotides has a unique mass (column 10, lines 9-12), and "through determination of the molecular weights of the four base-specifically terminated fragment families...the molecular weights of the four specifically terminated fragment families can be determined simultaneously by MS [mass spectrometry]...by running one reaction having all four chain-terminating nucleotides....comparison of the mass difference measured between fragments with the known masses of each chain-terminating nucleotide allows the assignment of sequence to be carried out" (column 5, lines 13-31).

Regarding method step I, Koster teaches "the invention utilizes the Sanger sequencing strategy," wherein the Sanger sequencing method is the amplification and synthesis of a target sequence with DNA polymerases and the incorporation of complementary dNTPs and ddNTPs (column 1, lines 61-67, through column 2, lines 1-8). Koster also teaches the incorporation of mass-matched and chain terminating nucleotides. Koster teaches "an amplification of the mass increment in mass-modifying the extended DNA fragments can be achieved by either using an equally mass-modified deoxynucleoside triphosphate (i.e. $dNTP^1$, $dNTP^2$) for chain elongation alone or in conjunction with the homologous equally mass-modified dideoxynucleoside triphosphate...ddNTP," wherein the superscript number indicates the position of the mass-modified nucleotide position (column 18, lines 22-31; and column 16, lines 63-67 through column 17, line 1).

Although Koster does not use the nomenclature "mass-matched," Koster uses the term "weight" as analogous to mass. Koster teaches mass spectrometry "weighs" individual molecules by ionizing them in vacuo and making them "fly" by volatilization

under electric and magnetic fields, and said ions "follow trajectories depending on their individual mass (m) and charge (z)....mass spectrometry has long been part of the routine physical-organic repertoire for analysis and characterization of organic molecules by the determination of the mass of the parent molecular ion" (column 5, lines 41-49). In view of Koster's teachings of "mass" and "weight," it is interpreted that the terms are interchangeable.

Regarding method step 2, Koster teaches calculating mass shifts of the incorporated nucleotides. Koster teaches mass shifts by the comparison of each nucleotide to that of a reference, wherein each nucleotide has a known weight, and the known target sequence has a calculated mass, wherein each incorporated nucleotide is compared to said reference (column 14, lines 53-67 through column 15, lines 1-7, Table 1 and Figure 6). Koster teaches the "correlation of calculated molecular weights...and their experimentally-verified weights....The molecular weight difference between two adjacent peaks can be used to determine the sequence," wherein the weight is measured in daltons (column 14, lines 67 and 68 through column 15 lines 1-5).

With respect to claim 2, Koster teaches "the use of mass-modified nucleoside triphosphate as chain elongators...for Sanger DNA...sequencing," wherein the mass-modified nucleotides are have identical mass-modified weights (column 17, lines 16-19 and column 18, lines 21-25).

With respect to claim 3, Koster teaches mass-matched nucleotides wherein it includes deoxyinosine triphosphate (dITP) (column 15, lines 66-67 through column 16, lines 1, and in view of claims 12 and 14).

and deoxyinosine triphosphate dITP (column 15, lines 66-67 through column 16, lines 1-3; Figures 8A and B, and in view of claims 11 and 12).

With respect to clam 12, Koster teaches mass-matched chain terminating nucleotides. Koster teaches ddNTPs "have each been mass-modified so as to have molecular weights resolvable from one another" (column 10, lines 35-41).

With respect to claim 13, Koster teaches a plurality of target nucleic acids is multiplexed in a single reaction measurement. Koster teaches "multiplex mass spectrometric DNA sequencing ...allow[s] simultaneous sequencing of more than one DNA...fragment," wherein said sequencing can occur in a single reaction (column 10, lines 59-61, and column 12, lines 23-25).

With respect to claim 14, Koster teaches mass-matched 7-deza-dG nucleotides. Koster teaches "nucleotides used for chain-elongation and/or termination are mass-modified. Examples of such modified nucleotides are...c7-deazanucleosides" (column 15, lines 66-67 through column 16, lines 1-3; Figures 8A and B, and in view of claims 12 and 14).

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-3 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 5, 7, and 8 of prior U.S. Patent No. 6,660,229. This is a double patenting rejection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 12 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9 and 10 of U.S. Patent No. 6,660,229. Although the conflicting claims are not identical, they are not patentably distinct from each other. Specifically, claims 9 and 10 of U.S. Patent No. 6,660,229 anticipates claim 12 of the instant application. Claim 12 discloses a general method of identifying

nucleotides in a plurality of target sequences by synthesizing extension products with chain terminating nucleotides, whereas claims 9 and 10 of U.S. Patent No. 6,660,229 discloses a specific method of determining a nucleotide sequence with by incorporating of chain terminating nucleotides and hairpin primers. Claims 9 and 10 fall within the scope of claim 12.

Claims 13 and 14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4 of U.S. Patent No. 6,660,229 in view of Koster (U.S. Patent No. 5,547,835). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1 and 4 of U.S. Patent No. 6,660,229 disclose a method of identifying a nucleotide at one or more positions with the synthesis of extension products with mass-matched nucleotides and the identification of each said nucleotide by calculating mass shifts of each extension product, wherein the mass matched nucleotides include mass-matched deoxynucleotide is deoxyinosine, 5-nitroindole, 3-nitropyrrole, 3-methyl 7-propynyl isocarbostyril, 5-methyl iscarbostyril or 3-methyl iscarbostyril. Claims 13 and 14 from the instant application differ in that it discloses a sequencing method comprising the synthesis of extension products with mass-matched nucleotides and the identification of each said nucleotide by calculating mass shifts of each extension product, wherein a plurality of target nucleotides are multiplexed in a singe reaction and the mass-matched nucleotides include 7-deaza-dG, phosphorothioate-7-deaza-dA, 5-propynyl-dU and 5-cyanomethyl-2'-deoxycytidine.

Koster teaches a sequencing method utilizing the analogs the c^7-deazanucleoside guanine (columns 15, lines 66-67 and column 16, lines 1-3, and in view of claims 12 and 14). Koster teaches that with modified nucleotides the skilled artisan can have "a further increase in throughput...by introducing mass-modifications in...chain-terminating nucleoside triphosphates and/or in the chain-elongating nucleoside triphosphates," wherein the modification can have "molecular weights resolvable from one another by the particular spectrometer being used" (abstract and column 10, lines 35-43). Koster also teaches that said reaction can "run[ing] one reaction having all four-chain terminating nucleotides...in one reaction vessel...By simultaneously analyzing all four base-specifically terminated reaction products, the molecular weight values have been, in effect, interpolated" (column 10, lines 23-28). One of ordinary skill in the art at the time the invention was made would have been motivated to have modified the methods of U.S. Patent No. 6,660,229 in view of Koster in order to achieve the benefit of performing a high-throughput sequencing method wherein each nucleotide base call can clearly be differentiated from another, and the flexibility of modifying said reaction to a particular type of spectrometer. The skilled artisan would have also been motivated to have modified the methods of U.S. Patent No. 6,660,229 in a single reaction to have an efficient means of sequencing and identifying each the four different nucleotides simultaneously as opposed to individually examining each nucleotide.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Wong whose telephone number is (571) 272-1120. The examiner can normally be reached on Monday-Friday; 8 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jennifer Wong

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